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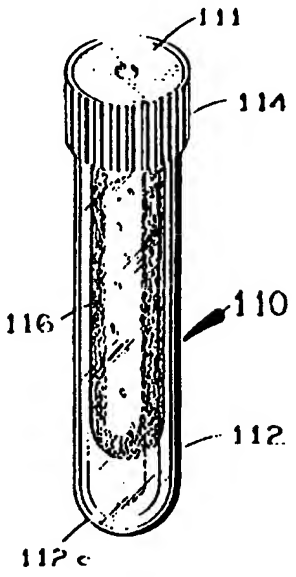
(57) Abstract

A multi-purpose device for sampling, collecting, recovering and storing of fluid samples, including recovery tube (12), a fluid absorbent medium comprising a cellular foam component (16), and a closure (14), which is physically coupled to the fluid absorbent element, and adapted to seal the fluid absorbent medium within the sample recovery tube. The sample recovery tube of this multi-purpose device comprises a resilient, preferably transparent, tubular member (12) having an open end and a closed end. The open end is provided with means for sealing engagement with the open end of a closure (14). In the preferred embodiments of this device, the closure is of composite construction and includes a vent or fluid channel (11) in the closed end thereof to permit access to a liquid or a gas within the sample recovery tube, and is yet essentially restrictive of fluid transfer under ambient conditions.



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SAMPLE COLLECTION, RECOVERY AND DISPENSING DEVICE FOR SALIVA

FIELD OF THE INVENTION

This invention is directed to a device for the collection, recovery and dispensing of a fluid sample, including biological fluid, such as saliva. More specifically, the instant invention is directed to a simple, yet effective device for collecting, recovery and dispensing of a fluid sample for on-the-spot testing and, optionally, for sample transport and/or archival retention. In one of the preferred embodiments of this invention, chemicals and/or a test strip is integrated within the sample collection device.

DESCRIPTION OF THE PRIOR ART

The analysis and testing of fluid samples for detection of constituents thereof generally involves initially obtaining a representative sample, and the transport of the sample to a laboratory for constituent analysis. Notable exceptions to this practice include the on-site collection and analysis of fluid samples (waste water samples for hazardous wastes) suspected of containing metals and carcinogens (qualitative testing); the breathalyzer tests administered by law enforcement for suspected drunk drivers; and, the self-administered testing of blood samples for glucose which are performed on a daily basis by diabetics. In each of the instances described above, the sample is collected via some expedient and transferred to an intermediate for storage and/or contact with one or more analytical reagents.

For example, in the testing of water samples suspected

of contamination by mercury a representative sample is initially obtained and placed in a suitable container and the container either sealed for later testing, or transported to a remote laboratory for testing. As is thus apparent, the vessel containing the sample must be both conservative of the sample and preferably adapted for later dispensing thereof to avoid any contamination of the sample and of the testing environment.

In the context of the constituent analysis of a biological fluid sample, the sample is typically collected by invasive procedures (e.g. finger stick or venous puncture of sample donor for a blood sample), or as a biological waste (e.g. urine or stool specimen), depending upon the analyte of interest, and the physical condition of sample donor. The traditional methods for the invasive collection of biological fluid samples (e.g. drawing blood) is generally restricted to certain controlled and/or laboratory environments. More specifically, the securing of a sample, such as by drawing blood, necessarily involves the consent of the subject, and is limited in terms of the size of the sample that can be obtained. Moreover, such invasive procedures generally require trained personnel to obtain the sample, and often result in a sample that is either of limited size and/or of limited stability. Alternative means of sample collection (e.g. voiding of a urine specimen) may prove to be an unacceptable option due to the unique attributes of a vital, biological fluid sample with respect to the constituents (analytes) of interest. More specifically, certain types of analytes (blood borne infections, cholesterol, triglycerides, blood alcohol, etc.) are not readily ascertainable from biological waste and, thus, there is no acceptable, alternative method for analysis other than one which employs a vital, biological fluid. Accordingly, the limitation imposed by the foregoing constraints restricts the clinician/investigator to either a vital biological fluid (blood or saliva) or, in the case of alcohol, to a

breathalyzer type test.

In the case of a breathalyzer type test, the sample obtained, by its very nature, is limited in the type of analyte that can be present therein, and is otherwise difficult to preserve and/or store. By way of contrast, a vital, biological fluid, such as saliva, is relatively easily obtained, stable, conveniently stored and contains a number of analytes of interest to both the clinician and to law enforcement. As is known, and common in saliva testing, the sample can be readily obtained by swabbing the buccal epithelial tissues in the donor's mouth, or through the use of a saliva collection device which is placed in the donor's mouth for a definitive period of time to allow for the adsorption of saliva thereon.

The collection of saliva, in the latter fashion, is preferred in that it protects the individual collecting the sample from exposure thereto, and otherwise provides a relatively sterile medium in which to transfer the sample for storage, or to subject the sample to analysis.

In order to further place the subject matter of this application in perspective, a number of patent references are discussed hereinafter as representative of the state of the art.

US Patent 5,334,502 (to Sangha), and the references cited therein, are fairly typical of the prior art for saliva collection, storage and testing. More specifically, the device described in the '502 patent (as illustrated in Figures 7 and 8) comprises an absorbent material in the nature of a wick, which is placed in the saliva donor's mouth, allowed to remain therein until essentially saturated, and, thereafter, is removed. In the device contemplated in the '502 patent, the absorbent wick is associated with a capillary tube, which surrounds the absorbent material and provides it with a degree of physical integrity. In the device illustrated in the '502 patent, an indicator is also provided within the device, which confirms the presence of saliva and other constituents therein. The device described in the '502

patent is purportedly useful for HIV testing and for drugs of abuse (to the extent present in the saliva).

Alternative embodiments of the saliva collection device of the '502 patent, (as illustrated in Figures 1 through 6) comprise a cotton swab which is used to collect and transfer a saliva sample from the mouth of the donor to a test site (absorbent sheet or layer), which contains an indicator that can interact with the saliva and/or constituents contained therein. As is apparent, and emphasized herein, the embodiments described in the '502 patent do not provide an effective means for both isolating and dispensing the sample and, thereafter, conveniently preserving the unused portion of the sample for later use and/or testing. More specifically, the use of a cotton swab is inherently incompatible with the collection and analysis of proteinacious analytes, or protein bound analytes, in that such materials adsorb (retain, interact, etc.) the protein and thereby prevent its later release for detection and analysis. Similarly, the indiscriminate teaching of the use of plastics (col 11, lines 13-21) as "absorbents" for saliva collection medium, is also flawed for the same reasons given above with respect to cotton. Notwithstanding the above and additional deficiencies in the teaching in the '502 patent, the use of saliva for constituent analysis has and continues to be the source of considerable interest and investigation because of the presence of numerous analytes in saliva and its accessibility as a test specimen. Unfortunately, the deficiencies in the techniques and devices for its collection has up to now postponed its widespread acceptance as the biological sample of choice.

Accordingly, there is, and remains, a continuing need to enhance the method by which saliva is collected from a donor and, thereafter, subjected to selective, diagnostic testing with the remainder thereof being stored for future use and testing (e/g/ confirmation testing in the case of drugs of abuse).

OBJECTS OF THE INVENTION

It is the object of this invention to remedy the above as well as related deficiencies in the prior art.

More specifically, it is the principal object of this invention to provide a simple, yet effective device for the collection, recovery and dispensing of fluids, including vital, biological fluid samples, such as saliva, which is both conservative of the sample and yet provides ease of access thereto for on-site testing and analysis.

It is another object of this invention to provide a simple, yet effective device for the collection, recovery and dispensing of vital, biological fluids, such as saliva, which includes a dispensing means integral with the device.

It is yet another object of this invention to provide a simple, yet effective device for the collection, recovery, testing and storage of vital biological fluids, such as saliva, which includes an optical window integral with the device to permit analysis of the sample within the device.

It is still yet another object of this invention to provide a simple, yet effective device for the collection, recovery and testing of vital, biological fluids, such as saliva, which includes one or more components of a sample analytical system within and/or integral with the device.

Additional objects of this invention include test kits and methods for on-site sample collection and testing of vital biological fluids, specifically test kits and methods for detection of infectious disease (HIV, HBsAG, etc.), drugs of abuse (cocaine, amphetamines, barbiturates, etc.) and therapeutic drugs (theophilin, digoxin, phenobarbital, etc.).

REFERENCE NUMERALS FOR FIGURES

For ease of understanding and continuity of expression, a numerical reference has been assigned to each component part of the device of this invention based upon the function of the component in the device. Thus, a component of a specific combination having the same function in the combination is present in a device of more

than one of the Figures, the last two numbers of the assigned reference numeral will be the same in each of the figures where such common function is illustrated. For example, in applying this convention to the functional component of the sample collection device designated as a "closure" (which is functionally designated with the numerical reference "14"), the closures of the collection device in each of Figures 5 and 6 are, thus, labeled with the reference numerals "514" and "614", respectively.

SUMMARY OF THE INVENTION

The above and related objects are achieved by providing a simple yet effective device for the collection, recovery, dispensing, testing and/or storage for fluid samples, such as saliva, which includes a sample recovery container (12) having an open end (12o) and a closed end (12c); a closure (14) having means (13) for engagement and sealing of the open end (12o) of the sample recovery container (12); and, a sample (e.g. saliva) absorbent element (16) affixed to the inner surface (e.g. internal webbing) of the closure (14) and extending therefrom into the sample recovery container (12). In the preferred embodiments of this invention, the sample recovery container (12) is a tubular member having an open end (12o) and closed end (12c); the closure (14) is adapted to engage and seal the open end (12o) of the sample recovery container; and, a sample absorbent element (16) is a bibulous member comprising a polymer foam of sufficient size and void volume to absorb a fluid sample which is recoverable therefrom in sufficient quantity to permit analysis and testing thereof without elaborate sample preparation or laboratory equipment and utilizing available methods and techniques.

In the preferred embodiments of this invention, the closure (14) includes a vent or channel (11) in the closed end (14c) thereof which permits access to a fluid within the tubular member 12. This vent or channel (11) in the closure (14) is essentially restrictive of fluid transfer

under ambient conditions, thus requiring that a negative or positive pressure be exerted upon the fluid within the tubular member to effect the passage thereof through the vent or channel (11) in the closure. In one of the alternative embodiments of this invention, the closure (14) is of composite construction, and is composed of an essentially open cylinder having an internal screw thread for engagement with a complimentary thread on the tubular container, and a closed end (14c) defined by a snap-in disk or accessory 15 also having at least one hole or channel (11) therein. This snap-in element (15) can take the form of a bottle dropper or have other functional attributes which are discussed herein.

It is both critical and essential to the efficacy of the device contemplated herein that the sample absorbent element (16) be matched to the physical and chemical properties of both the fluid sample and the analytes contained therein, in that it must be both capable of absorption and release of the sample and constituents of interest to allow for analysis thereof without any substantial interaction or adsorption thereof. In the preferred embodiments of this invention, the sample absorbent element (16) is an open cell polymer foam (prepared from a HYPOL brand urethane pre-polymer, available from W.R. Grace & Co., Boca Raton, FL) that is essentially inert (cross-linked) and otherwise unreactive (e.g. non-adsorbent) toward both the fluid sample and the analytes of interest within the fluid sample. This foam, (and other comparable materials), can be formulated, as desired, to have the requisite density and other physical properties consistent with the inherent characteristics of the absorbed fluid, and the contemplated method of sample recovery and analysis. In the preferred embodiments of this invention, the physical size and shape of the absorbent foam element (16) roughly parallels the shape of the chamber defined by the housing, and yet has a comparatively small profile (generally 50 to 60% of volume of the collection tube).

In a number of the alternative embodiments of this invention, the sample recovery component of the collection device comprises a tubular element (12) composed of a resilient elastomeric material and is preferably provided on the closed end (12c) thereof with functional tip (20) that includes a reservoir (19) which can collect the saliva if and when it is expressed from the sample absorbent element. In one of the alternative embodiments of the invention, the closed end (20c) of the functional tip (20) can be opened and thereafter resealed. This functional tip (20) is optionally provided with one or more indices (not shown), or graduation marks, corresponding to fluid volume, (analgous to a pipette), and, thus, can be used to dispense a metered amount of fluid (saliva) by simply squeezing the housing.

In another of the alternative embodiments of this invention, either the closure (14) and/or the functional tip (20) of the tubular element can be further modified to provide a fitting (18) for coupling or physically engaging (mating with) a fixture (21) which includes an analyte sensitive element (80). Thus, upon coupling of the collection device (10) and the fixture (21), it is thereupon possible to direct or focus the dispensing of the fluid contents of the collection device onto the analyte sensitive element within the fixture (21) to facilitate analysis thereof. More specifically, each of the closure (14) and/or the functional tip (20) of the sample recovery container of the collection device, and a fixture (21) for an analyte sensitive element can each be modified to engage the other so as to create leak proof union of the two and thereby provide a fluid pathway from the tubular element to a fluid receiving component of the fixture for the analyte sensitive element. Thus, subsequent to, or concurrent with, recovery of the fluid sample from the fluid absorbent element (16) (e.g. squeezing the foam) in the tubular member of the collection device, it can be directly applied from the reservoir within the sample recovery tube onto the

test element without any loss or inadvertent contact with the clinician. Moreover, since only the requisite amount of sample to perform the assay is used, the balance is conserved for re-testing or simply retained within the secure environment of the collection device, thus insuring against its cross-contamination and/or infection of unsuspecting individuals.

The volume of saliva that is collected by the fluid absorbent element (16) is a function of both the size of the absorbent element (16) and, of course, the time the element is in contact with the donor. A typical saliva collector of this invention has a fluid absorbent element (16) of sufficient size and fluid capacity to absorb and thereafter release (express) a sufficient volume of saliva (from about 100 to 200 microliters) for performance of at least one screening assay and at least one conformation assay (should that be required). As more fully set forth herein, the volume of sample contemplated for use in the solid phase immunoassays of interest will generally require at least 50, and preferably, 100 microliters.

The test kit of this invention, includes at least one analyte sensitive element and at least one sample collection device of this invention along with instructions for the performance of an analysis of the collected fluid sample. In an alternative embodiment of this test kit, one or more additional reagents can accompany the analyte sensitive element. More specifically, the preferred test kit of this invention includes a physically discrete fixture (e.g. having an analyte sensitive element) which is uniquely designed to be aligned and/or to couple with the foregoing sample device and thereby provide a direct and convenient means for transfer of the fluid contents from the collection device so as to permit its analysis.

Alternatively, the test kit can simply include an analyte sensitive element and/or interactive chemicals within a housing that is common to the sample absorbent element, wherein each are maintained isolated from the other until the appropriate time for transfer of the sample

to the analyte sensitive element.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig 1. is a perspective view of a preferred embodiment of a sample collection device of this invention;

Fig. 2 is an exploded view of the sample collection device of Fig. 1, which includes a sample recovery or collection tube and closure of composite construction;

Fig. 3A depicts an enlarged view of the composite closure of Fig. 2a, wherein the closed end of the closure comprises a disk insert having an orifice which defines a fluid pathway through the insert;

Fig. 3B depicts an enlarged top view of the open end (threaded member) of the composite closure of Fig. 3A.;

Fig. 4A depicts an alternative insert for the composite closure of Fig. 2A, wherein the insert is configured for dispensing an aliquot of sample from the collection device subsequent to its recovery thereof;

Fig. 4B depicts an alternative insert for the composite closure of Fig. 2A, wherein the insert includes a fitting that is configured for docking with a fixture which can include an analyte sensitive element;

Fig. 5 depicts a sample collection device wherein the closed end of the tubular component includes a skirt;

Fig. 6A depicts a sample collection device wherein the closed end of the tubular component includes pipette tip;

Fig. 6B depicts a sample collection device wherein the closed end of the tubular component includes a tapped dispensing tip having an internal pressure activated valve;

Fig. 6C depicts a sample collection device wherein the closed end of the tubular component includes a reagent tip and an accessory cuvette for uses in conjunction with the collection device;

Fig. 7A depicts an alternative embodiment of the sample collection device of Fig. 5, wherein the collection tube (12) is modified on the closed end thereof to accept an insert of the type illustrated in Fig. 4A;

Fig. 7B depicts an exploded view, in part, of the

sample collection device of Fig. 7A;

Fig. 8A depicts an alternative embodiment of the sample collection device of Fig. 5, wherein the collection tube is modified on the closed end thereof to accept an insert of the illustrated in Fig. 4B;

Fig. 8B depicts an exploded view, in part, of the sample collection device of Fig. 8A;

Fig. 9 depicts a sample collection device of Fig. 8A in docking relationship with a syringe;

Fig. 10 depicts the sample collection device of Fig. 5 in docking relationship with a Vacutainer-like syringe;

Fig. 11 depicts the sample collection device of Fig. 5 in cooperative relationship with a test icon;

Fig. 12 depicts an alternative embodiment of the sample collection device of Fig. 1 wherein the sidewall of the tubular component includes a reagent coating specific for interaction with one or more constituents of the sample;

Fig. 13 depicts the sample collection device of Fig. 1 in a "test kit;" and

Fig. 14 depicts the test kit of Fig. 13 in a "workstation" configuration.

DETAILED DESCRIPTION OF THE INVENTION INCLUDING PREFERRED EMBODIMENTS

As is discussed more fully herein, the design and operation of the various components of the sample collection device all cooperate to collect a fluid sample in sufficient volume as to be representative of the environment from which it has been obtained, and thereafter permit recovery of an aliquot of such fluid for constituent analysis. The device of this invention incorporates these multiple functions into a single, yet simple design. More specifically, the basic structure of the device (110) is illustrated in Fig. 1 and generally includes four (4) functional components, specifically a collection (sample recovery) tube (112), a closure (114) for the collection tube (112), a sample absorbent foam element (116) for collection (adsorption) of the liquid sample, (e.g. a biological fluids sample such as saliva) and a means (111)

for accessing the sample recovery chamber within the device (110) so as to permit dispensing of an aliquot of the sample without removal of the closure (114).

THE CLOSURE

As illustrated in the exploded view of this sample collection device (210) set forth in Fig. 2, the sample absorbent foam element (216) is integrated into the closure (214) and the closure (214) is of composite construction. The composite nature of the closure is further illustrated in Figs. 3A and 3B. More specifically, the closure (314) includes a closed end (314c) and open end (314o) which are structural and functionally unique.

The open end (314o) of the closure (314) is characterized as an essentially cylindrical element having means (313) for engaging and sealing the collection tube. In the embodiment of the device (210, 310) illustrated herein in Figs. 2 and 3, each of the collection tube (212,312) and the closure (214,314) is provided with a complementary thread (209). Moreover, the closed end (214c,314c) of the closure (214,314) is provided with a recess, or equivalent detente, (217,317) for acceptance of a disk-like insert (215,315). The insert (215,315) is complementary with the recess (217,317) in the closed end (214c,314c) of the closure (214,314) so as to form a locking seal between the insert and the recess/detente.

Alternative embodiments of this closure insert of Figs. 2 and 3 are depicted in Figs. 4A and 4B. More specifically, the closure insert depicted in Fig. 4A can take the form of a dropper bottle tip (415), and thus permit the dispensing of an aliquot of a recovered sample from the reservoir of the collection device onto an analyte sensitive element, or into a cuvette, for constituent analysis of the sample. Another embodiment of this invention contemplates a closure insert design which includes a fitting (418) adapted for docking with a fixture (432) for an analyte sensitive element that is capable of manifesting the presence of the analyte of interest, if present in the sample.

In each of the preferred embodiments of this invention, the closure insert (115) is designed to provide a less than air tight seal, or have a hole/channel (111) therein to permit the vapor and/or gas (e.g. air) that is trapped within the sample recovery tube (112) to be expelled at the time of expressing the sample from the sample absorbent medium into the sample recovery tube (112). Thus, in the context of this invention, the term "fluid" as used in conjunction with the terms "hole" and "channel," is inclusive of both liquids and gases. The size, shape and location of a hole/channel (111) in the cap allows for both the compression of the collection tube (112) during the recovery of the sample and its return to original shape. In each instance, the sample absorbent foam (116) remains firmly affixed to the internal structure of the closure (114).

SAMPLE ABSORBENT ELEMENT

As noted and once again emphasized herein, the device (110) of this invention, as depicted in Fig. 1, can be used in a variety of environments and thus its specific construction will be dictated accordingly. More specifically, where this device (110) is to be used to collect a fluid sample containing a hazardous waste comprising a highly acidic substance of organic substance, the materials selection for the components of the collection device (110) must be resistant to degradation by the sample. Similarly, where the device (110) is to be used in the collection of a biological fluid, such as saliva, the materials selection for the collection tube and the sample absorbent element (116) must be suitable to this task - inactive relative to proteins and constituents (collectively "analytes") of the sample. Moreover, where the device (110) is to be placed in contact with the donor, (e.g. in the donors's mouth), the sample absorbent element (116) cannot be ingested or subject to breakdown from the enzymes contained in the saliva or otherwise include any substance that can be leached from the element (116) during

the collection process or thereafter during the recovery of the sample from such element. The chemical and physical properties of the sample absorbent element (116) used in the collection of the saliva are thus critical to both the efficacy of the device, specifically the ability to absorb and thereafter release the biological fluid to allow for the analysis of the constituents contained therein.

In the preferred embodiments of this invention, the sample absorbent element (116) for a saliva collection device (110) of this invention is an inert (e.g. cross-linked) plastic which is prepared from a pre-polymer which is processed to produce an open cell foam having characteristics consistent with the foregoing sample collection and analysis requirements. In the preferred embodiments of this invention, the absorbent foam element (116) is formed of a water catalyzed polyurethane pre-polymer, of the type available from Hampshire Chemical Corporation, a subsidiary of W.R. Grace, under the HYPOL trademark.

These HYPOL brand polyurethane pre-polymers can be synthesized in accordance with the materials and procedures described in US Patent 3,903,232 (which is herein incorporated by referenece in its entirety). The processing conditions and composition of the foam are geared to provide a very high adsorption density (open cell foam) and sufficient tensile strength to withstand the rigors of sample collection and thereafter the recovery thereof by the compression of the foam so as to express the sample into the sample recovery tube where it can be contacted with an analyte sensitive element or dispensed onto a test strip analysis. Obviously this material must also be chemically inert (relative to the sample) and devoid of any unreactive and/or labile materials which can be ingested during the process of sample collection. In one of the preferred embodiments of this invention, this foam composition can be prepared from a hydrophilic cross linked polyurethane foam by interaction of an isocyanate terminated polyethylene polyol with large amounts of an

aqueous reactant. The resultant foams produced ther by can be molded to size and/or compressed. These foams are characterized as a low density polyurethane foam (one to about three pounds per cubic foot) which is readily compressible to about one-fifteenth to about one twentieth its original size.

These foams can be synthesized by initially capping (terminating) a polyoxyethylene polyol with an isocyanate. In brief, this process involves reacting a polyoxyethylene polyol with a polyisocyanate in a non-oxidizing atmosphere (nitrogen), at atmospheric pressure within a temperature range from about 0°C to about 120°C for a period of time of about twenty (20) hours, depending upon the temperature and the degree of agitation of the interactive constituents. The polyisocyanates used for capping the polyoxyethylene polyol include polyisothiocyanates, polyisocyanates which are PAPPI I(polyaryl polyisocyanate as defined in US Patent No. 2,683,730), tolylene diisocyanate, triphenylmethane - 4,4',4", triisocyanate, benzene-1,3,5-triisocyanate, hexamethylene diisocyanate, xylene diisocyanate, chlorophenylene diisocyanate, diphenylmethane-4,4'-diioscyanate, naphthalene-1,5-diisocy anate, xylene-alpha, alpha-diisothiocyanate 3,3'dimethyl-4,4'-biphenylene diiosocyanate,4,4'-methylenebis (Phenyl-isocyanate), 4,4'-sulfonylibis (phenylisocyanate), 4,4J-methylene diorthotolylisocyanate, ethylene diisocyanate, ethylene diisothiocyanate, trimethylenediisocyanate and the like. Mixtures of any one or more the above mentioned organic isothiocyanates or isocyanates may be used as desired. The aromatic diisocyanates and polyisocyanates or mixtures thereof which are especially suitable are those which are readily commercially available, have a high degree of reactivity and a relatively low cost.

Capping of the polyoxyethylene polyol may be accomplished using stoichiometric amounts of reactants. Desirably, however, an excess of isocyanate is used to ensure complete capping of the polyol. Thus, the ratio of

isocyanate groups to the hydroxyl groups used for capping is between about 1 to about 4 isocyanate to hydroxyl, and preferably about 2 to 5 about 3 isocyanate to hydroxyl molar ratio. In order to achieve an infinite cross-linked network formation on foaming the active components may be formulated in one of the following by way of example. First, when water is the sole reactant with the isocyanate groups leading to chain growth during the foaming process, the isocyanate capped polyoxyethylene polyol reaction product must have an average isocyanate functionality greater than 2 and up to about 6 or more depending upon the composition of the polyol and capping agent components. Secondly, when the isocyanate capped polyoxyethylene polyol has an isocyanate functionality of only about two, then the aqueous reactant may contain a dissolved or dispersed isocyanate-reactive cross-linking agent having an effective greater than two. In this case, the reactive cross linking agent is reacted with the capped polyoxyethylene polyol when admixed during and after the foaming process has been initiated. Thirdly, when the isocyanate capped polyoxyethylene polyol has an isocyanate functionality of only about two, then a polyisocyanate cross-linking agent having an isocyanate functionality greater than two may be incorporated therein, either preformed or formed in situ, and the resultant mixture may then be reacted with the aqueous reactant, optionally containing a dissolved or dispersed reactive isocyanate-reactive cross-linking agent, leading to a cross-linked, infinite network hydrophilic polyurethane foam.

In the context of this invention, the sample absorbent element is formed by simple and well-known fabrication methods. For example, foams can be formed for fluid sample absorbent element of this invention from the foregoing HYPOL like pre-polymers, utilizing techniques analogous to those described in US Patent 4,944,947 (to Newman), which is incorporated by reference in its entirety. More specifically, Newman patent describes fabrication of a dental appliance from a HYPOL foam pre-polymer (HYPOL FHP-

2002), which is simply added to an aqueous medium at an elevated temperature (110°F,38°C), and thereafter stirred vigorously until frothy. A given amount of this mixture is then cast into molds which have been pre-heated to 100°F, the molds clamped closed and the polymer permitted to cure (cross-link). After an abbreviated period, the molds are opened and the molded foam article is removed. Curing of the foam continues until the cross-linking reaction has gone to completion.

In one of the embodiments of this invention illustrated in Fig. 3B, the closure (314) is initially affixed to the mold (not shown) and the sample absorbent element (316) formed by injection of the foam into a mold through the top of the closure (314). As the foam expands, it fills the mold and flows into the closure. Sufficient foam is charged to the mold to cause the expansion thereof into the closure (314) so as to become entrained by webbing within the closure (314) where it remains affixed to the webbing upon curing.

SAMPLE RECOVERY TUBE

As illustrated in Figs. 1 and 2, the sample recovery tube (112,212) of the collection device (110,210) of this invention can have a simple round bottom configuration, depending upon its intended uses, a flexible (and resilient) sidewall construction and versatility for configuration with other functional components of the device. In another of the alternative embodiments of this invention, the sample recovery tube (112) can be prepared from a relatively rigid material, (e.g. thermoset plastic). In each of the embodiments of this invention, the sample recovery tube (112) has an open end (112o) and a closed end/or sealed end (112c). The open end (112o) is of sufficient diameter to accommodate the insertion and removal of the sample absorbent element (116), and is further provided with external threads, or an equivalent expedient, for sealing engagement by a screw cap or comparable closure (114).

By way of contrast, the sample collection device (510) illustrated in Fig. 5 comprises a skirted tube (512). As more fully illustrated in these accompanying Figures (Figs. 5 to 8 inclusive), the closed/sealed end of the sample recovery tube (512) of the collection device (510) of this invention can include various means for accessing the fluid from within the tube, and for resealing the closed end of the sample recovery tube after an aliquot of the sample has been obtained.

For example, in the device (610) illustrated in Fig. 6A, the sample recovery tube (612) is provided on the closed end (612c) thereof with a dispensing tip (620) that can be opened and resealed. The tip can be re-sealed by simply heating the tip until it melts, or with an appropriate closure designed for that purpose. The inclusion of an internal pressure activated valve (621) of the type shown in Fig. 6B eliminates the need for re-sealing of the dispensing tip (620). More specifically, upon exertion of pressure on the contents of the sample recovery tube (612) the valve (621) is forced to open and thereby permits the flow of fluid from within the sample recovery tube. In the absence of such pressure, the dispensing tip (620) remains sealed and the contents of the tube secure.

Fig. 6C depicts yet another alternative embodiment of the sample recovery tube (612) wherein a distinct chamber (622) is formed in the closed end of the sample recovery tube. More specifically, the closed end (612c) of the sample recovery tube (612) can be modified as illustrated in Fig. 6C to incorporate a plurality of septa (623,624) to define one or more chambers (622) at or near the terminus (620) of closed end (612c) of the tube (612). A typical chamber can contain a liquid material (624) (e.g., chemistry system) specific for interaction with a constituent of the sample incident to the analysis thereof; and/or to supplement the volume or dilute the sample. This latter embodiment of the invention further contemplates the uses of an additional accessory in the nature of a cuvette (625) which, in the embodiment of the

invention depicted in Fig. 6C, includes a piercing member (e.g. needle) (626) to puncture the septa (623,624) of the chamber(s) (622) in the dispensing tip (620) and thereby cause the sample and the contents of the chamber (624) to commingle and flow into the cuvette (625) where they are combined. To the extent necessary or appropriate, the sample recovery tube (612) can be squeezed to assist the flow of fluid through dispensing tip into the cuvette (625). The cuvette (625) used in this embodiment of the invention can comprise a rigid device which includes an optical window (626), or be composed of resilient material that is compliant with a read station of a monitoring instrument (not shown).

As noted above, and once again emphasized, the sample recovery tube (112) of the collection device (110) of the type depicted in Fig. 1 is preferably of a flexible side-wall construction, and transparent to allow for observation of the sample within the sample recovery tube (112). Thus, once the sample has been collected on the sample absorbent element (116) and this element inserted in the tube, the tube is sealed with the closure (114). In the preferred operation and use of the sample collection device of this invention, the sides of the sample recovery tube are squeezed so as to compress the sample absorbent element therein and thereby express the sample from the sample absorbent element into a reservoir (112r) provided at the closed end (112c) of the sample recovery tube (112). Once the sample is expressed, the orientation of the tube, and the distance between the tube and foam, prevents the re-contact of the foam with the sample in the reservoir.

Obviously, it is desirable from both a consumer and manufacturing perspective to provide one or more basic designs for the sample collection device of this invention and yet permit the adaptation thereof to a particular application or user preference without departure from such basic design concept(s). As depicted in Fig. 1, and discussed herein, one means for imparting such versatility

can be achieved with a universal closure (114) design which lends itself to user adaptation to a specific need or preference by simply interchanging the snap-in insert of choice.

As illustrated herein in Fig. 7, comparable versatility in the sample collection device (710) can be achieved with a universal sample recovery tube design (712,812) of composite construction which lends itself to user adaptation to a specific need or preference by substitution of the conventional sample recovery tube (112) of unitary design for a design with interchangeable snap-in inserts for the closed end (712c,812c) of the sample recovery tube (712,812). As depicted in Fig. 7 and 8, the sample recovery tube (712,812) can comprise a composite characterized by an elongate barrel having an open end (712o,814o) and a closed end (712c,814c). The open end (714o,814o) of the tube is essentially the same as the tube of unitary structure depicted in Fig. 1 (e.g. external threads for engagement with a screw cap) and further includes means for modification of the closed end (712c,812c) with any one of a number of snap-in inserts of the type described herein for the composite closure (114,214,314) depicted in Figs. 2,3 and 4 respectively. In its simplest form, the composite sample recovery tube (712,812) of the collection device (710,810) of this invention can have a solid member as snap-in insert (770,870) in the closed end (712c,812c) thereof , which can be replaced with a functional accessory, as appropriate. More specificaly, the closed end (712c,812c) of the sample recovery tube (712,812) illustrated in Fig. 7 and 8 is provided with a recess or detente (717,817) formed within the barrel of the tube at the terminus of the tube. This recess/detente (717,817) is designed to receive a snap-in insert (715,815) which can include a functional accessory (e.g. dispensing tip) of the type depicted in Fig. 7A and B or, alternatively, the snap-in insert can include a fitting (718,818) designed for docking with a fixture and/or a syringe such as is depicted in Fig. 4B and Fig. 9

respectively. In each instance the choice of insert can tailor the utility of the sample collection device (710,810) to the particular needs and environment contemplated for its use.

In the embodiment of this invention illustrated in Fig. 9, the sample collection device (910) of this invention is provided with a closure (914) of composite construction, which includes a fitting (918) adapted for docking with a syringe (950). Once the syringe (950) has been docked with the fitting (918) of the device, the contents of the syringe can be injected into the sample recovery tube (912) or, alternatively, the sample is accessed from the sample recovery tube (912) through the closure, by the syringe. As noted and once again emphasized, this fitting can be designed for docking with any one of a number of complimentary devices and/or accessories which permit access to the sample without removal of the closure (914) or piercing of the sample collection device.

In those instances where the physical integrity of the sample collection device is not of concern, the sample can be accessed from within the sample recovery tube by piercing the tube with a hypodermic needle/syringe setup. More specifically, the syringe used in the embodiments of this invention, once equipped with a hypodermic needle can easily puncture the tube and/or be inserted through the hole/channel in the closure to withdraw fluid from within the sample recovery tube. In this latter embodiment of the invention, the foam that is entrained within the webbing of the closure functions much in the same way as septa of a vial, by permitting insertion of the needle into the tube and yet effectively re-sealing the tube at the time the needle is withdrawn.

In the configuration depicted in Fig. 10, a Vacutainer-type syringe is placed in proximate relation to the closed end of the sample recov ry tube and upon puncture of the container effects withdrawal of sample from

within the sample recovery tube. More specifically, once the sample has been recovered from the sample absorbent element, it can thereafter be accessed from the sample recovery tube (1012) by simply puncturing the closed end (1012c) of the tube with a needle (1026) associated with a syringe (1050) and an aliquot of the sample withdrawn through the needle into a syringe. In the embodiment of the syringe illustrated in Fig. 10, the barrel (1051) of syringe (1050) is under a negative pressure thereby effecting withdrawal of the sample. As an aliquot of the sample is withdrawn from the sample recovery tube (1012), the tube (1012 will deform thus permitting an uninterrupted flow of sample into the syringe (1050).

Alternative methods for accessing an aliquot of the sample from the sample recovery tube, as depicted in Fig. 11, include the provision of a needle (1126) integral with a test device (1160) which houses an analyte sensitive element. In this embodiment of the invention illustrated in Fig. 11, a skirted tube of the design shown in Fig. 5, is placed in registration with alignment means (1175) of a test device. As the sample recovery tube (1112) of the collection device (1110) and test device (1160) are each coupled to the other, the needle (1126) in test device punctures the closed end (1112c) of the sample recovery tube. An aliquot of the sample is thereby accessed and can be applied to the analyte sensitive element by simply squeezing the sample recovery tube (1112) so as to cause the sample to flow down the grooves (not shown) in the needle and thereby initiate an analyte manifesting reaction within the analyte sensitive element in the test device.

In yet another alternative embodiment of the invention depicted in Fig. 12, the interaction of the constituents of the sample with analyte manifesting reactants can be accomplished entirely within the sample recovery tube (1212), without removal of the closure (1214) from the sample collection device (1210), by initially coating such reactants (1280) on the interior sidewall of the tube at the time of assembly and thereafter drying such reactants

(1280) on the interior sidewall of the tube at the time of assembly and thereafter drying such reactants on the tube wall. It is also understood that the constituents in the sample may be measurable due to some intrinsic property, or alternatively, are manifest once having been combined with another substance which is present in the collection tube (1212) and/or added to the collection tube. More specifically, chemical substances (1280) can be coated on the interior of the collection tube (1212) and freeze dried. Upon introduction of the sample absorbent medium into the tube and the recovery of the fluid absorbed thereof by squeezing the sidewalls thereof in the direction indicated by the arrows, the chemicals are reconstituted and interact with the analyte of interest in the sample to produce a discernible change therein which is indicative of the analyte of interest. Alternatively, the chemicals can be present as an encapsulant (e.g. frangible microspheres) on the interior of the collection tube (1212). Thus, upon squeezing of the sidwalls of the tube incident to recovery of the sample from the sample absorbent medium, these microspheres (1280) are ruptured and the chemical agents contained therein are released and interact with one or more constituents in the sample to produce a detectable species that is indicative of the presence of the analyte in the sample.

Thus, subsequent to collection and upon expressing the sample from the sample absorbent medium (1216) within the tube (1212), the reactants are reconstituted by the sample and thereupon interact with the constituents of the sample so as to produce a discernible change within the sample recovery tube (1212) that is indicative of the analyte of interest. This discernible change within the tube (1212) can include the formation of a distinctive color, increase in the turbidity in the fluid phase of the sample, formation of bubbles, formation of a precipitate, and or/ a combination of both.

Similarly, chemical agents can be entrained within the

sample absorbent medium and not released unless and until the appropriate sequence in the analytical process. Obviously, where the sample is a biological fluid such as saliva, the use of chemical reagents in the tube and/or in conjunction with the absorbent medium must be approached with caution.

SAMPLE COLLECTION AND RECOVERY

In the contemplated use and operation of the device of this invention, the sample is obtained by contact (or immersion) of a sample absorbent medium with a source of a fluid suspected of containing an analyte of interest. In the context of analysis of waste water for a toxic substance (e.g. heavy metals, organic, etc.), a representative sample of the waste water is obtained and the sample absorbent medium simply immersed within the sample. The amount of the sample that need be absorbed to perform the desired analysis is determined utltimately by the analytical protocol, and it is assumed this immersion procedure will supply more than adequate sample for the intended analysis.

Alternatively, where the device of this invention is to be used to collect a biological fluid sample (e.g. saliva) through contact of the sample absorbent medium with a sample donor, the contact must be of sufficient duration to allow for adsorption of a representative sample and, preferably, be obtained under "normal" conditions (as compared to a saliva sample that is through the use of flavored element - "stimulated" sample).

In the context of constituent analysis of saliva, with device of the design of Fig. 1, the sample absorbent medium of the device (110) of this invention can be readily adapted to the age of the donor (infants, toddlers, adults) and otherwise have varying porosity to make it more or less absorbent. Alternatively, this device (110) can be used with the other traditional biological fluids, (e.g. urine, whole blood, serum, etc.) and its design may thus vary accordingly. In each instance, the sample is obtained by first removal of the sample collection element (116) from

its secure environment within the collection tube (112), the sample collected as above described and the sample collection element (116) sealed within the collection tube. Assuming that an adequate (by volume) sample has been obtained, it can thereafter be expressed by any one of a number of techniques, depending upon the configuration of the device (110) of this invention, and once recovered, subject to constitutent analysis.

Again, depending upon the specific configuration of the device of this invention, the collection and recovery of a representative sample of fluid is accomplished with relative ease and security. Although not generally recommended when dealing with samples containing a toxic and/or infectious agent, the closure obviously can be removed from the device to permit access to the sample with the sample recovery tube, and an analyte sensitive element and/or chemicals added into the sample recovery tube and allowed to interact with the recovered sample. This method of analysis is generally undesirable since it needlessly exposes the clinician and the environment to the used sample absorbent element and the contents of the sample recovery tube.

Where the sample is, however, suspected of containing infectious organisms, the preferred embodiment of the device selected will insure that once the sample has been obtained, it is retained within the secure environment of the collection tube and thereafter only supplied for analysis in a manner that prevents contamination of the ambient environment and those persons that must have access thereto for purposes of analysis.

Where the device of this invention does not afford access to the sample via a dispensing orifice integral with the device, or other means, the sample is generally obtained by first expressing the sample from the sampl absorbent foam element into a reservoir at the closed end of the sample recovery tube, and then removing the closure from opening of the sample recovery tube of the collection

device, (which also results in the sample absorbent element withdrawn from the recovery tube). An aliquot of fluid sample can thereafter be withdrawn from the sample collection tube with a pipette, or the sample simply transferred to another vessel for analysis, by pouring the sample from the tube into the test vessel. After at least some of the sample has been removed from the tube, the sample absorbent element and the closure are re-united with the sample recovery tube and the tube sealed with the closure.

The flexible sidewall design of the collection tube permits the recovery of the sample from the sample absorbent foam element by compressing the foam within the tube, where it collects in the reservoir in the bottom (closed end) of the tube. During this process of sample recovery, the volume of air confined within the tube is preferably displaced to allow for ease of compression of the sample recovery tube and the squeezing of sample absorbent foam element within the tube to be readily and most efficiently collection compressed. Where such confined air cannot be safely vented and, thereafter the tube caused to re-expand, the sample recovery process is inefficient, requires substantial pressure to squeeze the tube and express the sample, can cause potential damage to the tube and to the closure and generally recovers less sample from the sample absorbent element. The provision of a vent/channel in the closure dramatically improves the sample recovery process without compromising the sealing of the device or requiring excessive squeezing of the collection tube, thus minimizing the potentiality for damage to collection device during the sample recovery process.

As is apparent from the above, the collection and recovery of the sample within the device of this invention is only the beginning of the process for the determination of the presence of the analyte of interest, and, in some instances, the amount thereof. In order to accomplish such analysis, an aliquot of sample is contacted with an

analyte sensitive el ment that is specific for the manifestation of the presence of the analyte of interest. In its simplest form, the analyte sensitve element can be one or more chemicals that are reactive with the analyte of interest, or alternatively, an elaborate chemistry system. In each instance, the analyte sensitive element can be contacted directly with the sample by the placement thereof into the collection tube, or an aliquot of sample withdrawn/dispensed from the sample recovery tube and reacted with the analyte sensitive element in a test environment that is independent of the collection device of this invention. In the simplest embodiment of this invention, an aliquot of sample can be removed from the sample recovery tube through the use of a pipette or straw. As noted above, the preferred sample handling routine involves the use of one or more of the accessory inserts to modify the closure or the sample recovery tube to enable dispensing of a recovered sample without removal of the closure and the sample absorbent element from the sample recovery tube.

ANALYSIS OF SAMPLE

Typically, the sample recovered with the device of this invention can be subjected to analysis by one or more test protocols for determination of the presence and/or amount of the constituents of interest. In the performance of such analysis, a test kit (1300) of the type in the illustration in Fig. 13 is provided which generally includes the sample collection device (1310) and all of the accessories (e.g. unit packages of reagents) (1380) and reagent system (1360) needed to complete the desired analysis. The manner in which such components are arranged and presented is often critical to proper and consistent test results, particularly when such test is to be performed by relatively unskilled personnel and at a location remote from a clinical laboratory. Accordingly, this invention includes, as illustrated in Fig. 14, a test kit package (1400) which provides a series of recesses

(1490) and instructions associated with the package for arranging the kit components in a "work station" format to insure proper sample and reagent utilization and consistent test results.

EXAMPLES

The Examples which follow further define, describe and illustrate the various embodiments of this invention. Parts and percentages appearing in such Examples are by weight unless otherwise indicated. Apparatus and equipment used in the fabrication and evaluation of the sample collection of this invention are standard unless otherwise indicated.

Example I

1. Fabrication of Sample Collector - A sample recovery tube is initially obtained from Precision Laboratory Plastics (Centrallia, WA). This tube has a flexible sidewall, is essentially transparent, closed on one end and open on the opposite end. This sample collection tube is approximately 3 inches in length and has an inside diameter of 0.5 inches. The open end thereof is provided with external threads for sealing engagement with a closure (screw cap) of the type depicted in Figure 3.

A sample absorbent element is prepared by molding a hydrophilic polyurethane foam compound (HYPOL FHP 2002, available from W.R. Grace, Boca Raton, FL), utilizing the tube of the collection device as a form. More specifically, a foam element is fabricated by injection of a foam compound through the open end of the closure into the collection tube, allowing the foam to expand within the tube and into the webbing of the closure. As the foam cures, it shrinks within the tube, thereby providing a space between the sample absorbent foam and the sidewall of the tube. The foam also shrinks in the long dimension thereby providing a reservoir in the end of the tube for the collection of sample. The shrinkage of the foam does not affect its attachment to the webbing of the closure, where it remains anchored. A snap-in cap (insert) is thereafter inserted into the top of the closure to complete

the device.

The HYPOL foam compound selected for this application is formulated to shrink approximately 40%, thereby permitting the absorbent element to be easily withdrawn and reinserted into the tube incident to the sample collection process. Since the absorbent element is integral with the closure, it does not require any further processing to secure it. Once the foam has sufficient green strength, the cap and the foam element can be removed from the tube and inserted into the saliva donor's mouth and allowed to absorb saliva.

2. Collection of the Sample - After the device has been fabricated in the above manner, it can be used to obtain a fluid sample for preservation and/or analysis. Initially, the closure and sample absorbent foam is removed from the device by simply unscrewing the closure from the collection tube. The sample collection process can simply involve the immersion of the foam into a fluid sample or by the contact of this foam with a sample donor. In the context of saliva collection, this foam element is placed in the donor's mouth and allowed to remain in contact with salivary secretions for an abbreviated period of time (generally 3 to 5 minutes). It is important to emphasize that the salivary secretion is collected under normal conditions and that the donor's salivary glands are not stimulated by prior contact with food or other artificial means. After sufficient saliva (at least 75 to 100 micro liters) has been absorbed by the fluid absorbent foam, the foam is removed from the donor's mouth, placed in the collection tube and the tube seal as before with the closure. The sample can thereafter be recovered by simply squeezing the flexible sidewall of the collection tube. The physical properties of the recovered sample closely approximate those of water (saline) and thus further analysis thereof can be accomplished without any additional sample preparation or treatment.

3. Sample Analysis - Once the sample has been

collected and recovered in the manner described above, it can be subject to analysis and testing by contacting an aliquot thereof with one or more components of a diagnostic test kit, e.g. immunoreagents specific for interaction with one or more constituents of the sample. Typically, these additional kit components include an analyte sensitive element (Test Strip) and one or more additional reagents, depending upon the assay format and analyte of interest.

Diagnostic Test for HIV Antibodies

In a diagnostic test for determination of the presence of antibodies indicative of the AIDS virus (HIV), the analyte sensitive element comprises an HIV specific binding protein immobilized within a membrane that is supported in a housing. The HIV specific analyte sensitive element is available commercially, for investigational use, from Technical Chemical & Products, Inc. (TCPI), Ft. Lauderdale, Florida (Rapid brand).

In the TCPI diagnostic test for the analysis of saliva for antibodies to the HIV virus, the analyte sensitive element is fabricated from a nitrocellulose membrane (Millipore Corp.) backbone support that is spotted with the specific antigen fragments (i.e. p120, gp40) that are bound to the membrane after the membrane has been prepared to accept the antigen mixture. The membrane is first pre-wet with a phosphate buffer to activate the surface and prepare it to accept the antigen solution. The antigen mixture is dispensed onto the membrane (2-5 microliters) so as to form a spot of 0.5-3mm in diameter. The spot is then allowed to dry either naturally or in a vacuum drying oven. The antigen spotted membrane is thereafter immersed in a solution containing a wetting agent and a protein (BSA or Casein) to block the unreactive sites. The resultant HIV specific membrane is then dried as above. The dried membrane is mounted in a holder which contains a molded-in well and absorbent pad for absorption of excess sample.

In use, the mounted membrane is first pre-wet with a buffer solution which is then allowed to completely absorb into the membrane and its underlying absorbent pad. The

next step is the addition of a colloidal gold-protein A conjugate solution. One hundred (100) microliters of this conjugate solution is added to the test well and allowed to absorb by the membrane. The final step is the addition of a wash solution whose purpose is to clarify and accentuate the positive result if present. A positive result is visualized by the gold solution coupling to the antigen-antibody complex formed when a positive antibody sample is placed in contact with the spot of antigen on the membrane and turning it red. If no antibody is present (a negative sample) then there is no complex formed and thus the gold solution does not bind and no red spot is visualized.

Diagnostic Test for Hepatitis Antigen (HBsAG)

In a diagnostic test for determination of the presence of antigen indicative of infectious Hepatitis (HBsAG), the analyte sensitive element comprises a linear test strip having a series of zones, each specific for performance of a discrete function. The analyte sensitive element is available commercially, for investigational use, from Technical Chemicals & Products, Inc., Ft. Lauderdale, Florida (**Rapid** brand One-Step test format).

The analyte sensitive element comprises a sample pad which is integrated with and/or in fluid communication with a test strip (nitro cellulose membrane). The sample collection pad is of sufficient void volume to accommodate adequate sample to perform the contemplated assay. The functional areas of the membrane include a reagent zone within which is deposted (and lyophilized) an unbound (mobile) gold labeled antibody conjugate specific for interaction with the analyte of interest (HBsAG). Thus, upon application of the sample to the analyte sensitive element, the sample reconstitutes the gold labeled conjugate and thereby provides a medium for the interaction between the analyte and the conjugate, so as to form an immunocomplex. As the sample is absorbed by the test element, it causes this immunocomplex, and any excess (unreacted) conjugate, to pass along the fluid pathway

within the test element where it comes in contact with an immobilized binding substance (e.g. antibody) specific for interacting with and which includes one or more delimited areas having an immobilized binding material specific for the interaction with a constituent of a biological fluid sample or a reaction product which includes a constituent of the biological fluid sample. The analyte sensitive medium is preferably mounted in a fixture with other accessory components to assist in the distribution and flow of the biological fluid sample within the analyte sensitive element. The format of the analyte sensitive medium suitable for use in this invention can accommodate amounts of fluids generally in excess of that required to perform the assay so as to permit its use in the home health care (self-testing) environments.

What is claimed is:

1. In a device for the collection, recovery and storage of a fluid sample, including a sample collection ensemble comprising (i) a porous sample absorbent medium for contact and adsorption of a fluid sample, which medium is characterized as having a geometry consistent with removal and insertion thereof into a container intended for use in conjunction therewith, (ii) a sample recovery container comprising an elongated tubular member having an open end and sealed or closed end which is further characterized as comprising an essentially transparent elastomeric material and (iii) a closure for sealing engagement with the open end of the sample recovery container, said closure being physically associated with and supportive of the porous sample absorbent medium,

wherein the improvement comprises:

access means associated with one or more components of a sample collection device which permit withdrawal of a liquid and/or the expulsion of a gas from within a sample recovery container of said device without removal of the closure from, or otherwise unsealing, the open end of the sample recovery container of said device.

2. The improvement of Claim 1, wherein said access means is selected from the group consisting essentially of

(a) means which are integral with at least one of the sample collection device, and

(b) a composite, which includes

(i) means associated with the closed sample recovery container for sealing engagement with an accessory insert; and

(ii) an accessory insert adapted for sealing engagement with said sealing engagement means of the closed sample recovery container, said accessory insert being readily interchangeable with another of

similar or alternative design, and being further characterized as either having no other function than to seal the closed container or as having a fluid channel adapted for permitting access to the contents of the sample recovery container through said channel, to permit expulsion of a gas and/or access to a liquid from within said container, upon the exertion of pressure upon the sample recovery container.

3. The improvement of Claim 2, wherein the access means can be integral with the closure or the sample recovery container.

4. The improvement of Claim 2, wherein the access means can comprise a composite closure wherein said accessory insert is disposed in the closed end of the closure.

5. The improvement of Claim 2, wherein the access means can comprise a composite sample recovery container wherein said accessory insert is disposed in the closed end of the sample recovery container.

6. The improvement of Claim 2 , wherein the access means comprises a bayonet mount type fitting.

7. The improvmeent of Claim 2, wherein the access means comprises a threaded fitting.

8. The improvement of Claim 2, wherein the access means comprises a valve that opens upon mating engagement of the coupling with the fixture and re-seals upon disengagement of the coupling and the fixture.

9. The improvement of Claim 2, wherein the tubular member of the sample recovery container includes at least two chambers, and means for physically isolating each of the chambers from the other.

10. The improvement of Claim 9, wherein said isolation means is capable of physical displacement or rupture, under assay conditions, to allow for flow of a

fluid sample from one chamber to another.

11. In a device for the collection, recovery and storage of a biological fluid sample, including a sample collection ensemble comprising (i) a porous sample absorbent medium for contact and adsorption of a fluid sample, which medium is characterized as having a geometry consistent with removal and insertion thereof into a container intended for use in conjunction therewith, (ii) a sample recovery container comprising an elongated tubular member having an open end and sealed or closed end which is further characterized as comprising an essentially transparent elastomeric material and (iii) a closure for sealing engagement with the open end of the container, said closure being physically associated with and supportive of the porous sample absorbent medium,

wherein the improvement comprises

a closure of composite construction having an open end and a closed end, including

(i) a means for physically engaging the open end of said closure with the open end of an elongated tubular member of a sample collection ensemble so as to effectively seal the open end of the elongated tubular member in relation to the open end of the closure; and

(ii) a fluid channel associated with the closed end of said closure for permitting the expulsion of a gas and/or access to a liquid from within said elongated tubular member, said channel being further characterized as essentially restrictive of fluid transfer under ambient conditions.

12. The improvement of Claim 11, wherein the closure includes a coupling means for matingly engaging a fixture so as to facilitate the dispensing of an aliquot of sample from the container relative to said fixture.

13. The improvement of Claim 12, wherein the coupling

means includes a fluid channel so as to provide an essentially continuous fluid pathway from the interior of the elongated tubular member to a cavity within said fixture.

14. The improvement of Claim 12, wherein the coupling means comprises a tapered fitting.

15. The improvement of Claim 12, wherein the coupling means comprises a luer lock type fitting.

16. The improvement of Claim 12, wherein the coupling means comprises a bayonet mount type fitting.

17. The improvement of Claim 12, wherein the coupling means comprises a threaded fitting.

18. The improvement of Claim 12, wherein the coupling means comprises a pressure activated valve that opens upon mating engagement of the coupling with the fixture and re-seals upon disengagement of the coupling and the fixture.

19. The improvement of Claim 13, wherein the cavity of said fixture contains an analyte responsive element selected from the group consisting essentially of a solid, liquid or a gas.

20. The improvement of Claim 19, wherein the analyte responsive element includes a liquid absorbent medium and at least one reagent that is interactive with a constituent of the sample, an immunocomplex of an additional material and a constituent of the sample or a reaction product of the sample and an additional material.

21. In a device for the collection, recovery and storage of a biological fluid sample, including a sample collection ensemble comprising (i) a porous sample absorbent medium for contact and adsorption of a fluid sample, which medium is characterized as having a geometry consistent with removal and insertion thereof into a container intended for use in conjunction therewith, (ii) a sample recovery container comprising an elongated tubular member having an open end and sealed or closed end which is further characterized as comprising an essentially transparent elastomeric material and (iii) a closure for sealing engagement with the open end of the container, said

closure being physically associated with and supportive of the porous sample absorbent medium,

wherein the improvement comprises

a sample recovery container of composite construction having an open end and a closed end, including

(i) a means for physically engaging the open end of said container with the open end of a closure so as to effectively seal the open end of the container in relation to the open end of the closure;

(ii) means associated with the closed end of the container for sealing engagement of an accessory insert; and

(iii) an accessory insert adapted for sealing engagement with said sealing means on the closed end of the sample recovery container, said accessory insert being readily interchangeable with another of similar or alternative design, said insert being selected from the group consisting of an insert having no other function than to seal the closed end of the container and an insert having a fluid channel adapted for permitting access to the contents of the container through said channel, so as to permit expulsion of a gas and/or access to a liquid from within said container.

22. The improvement of Claim 21, wherein the sample recovery container includes a coupling means for matingly engaging a fixture so as to facilitate the dispensing of an aliquot of sample from the container relative to said fixture.

23. The improvement of Claim 22, wherein the coupling means includes a fluid channel so as to provide an essentially continuous fluid pathway from the interior of the elongated tubular member to a cavity within said fixture.

24. The improvement of Claim 22, wherein the coupling

means comprises a tapered fitting.

25. The improvement of Claim 22, wherein the coupling means comprises a luer lock type fitting.

26. The improvement of Claim 22, wherein the coupling means comprises a bayonet mount type fitting.

27. The improvement of Claim 22, wherein the coupling means comprises a threaded fitting.

28. The improvement of Claim 22, wherein the coupling means comprises a pressure activated valve that opens upon mating engagement of the coupling with the fixture and re-seals upon disengagement of the coupling and the fixture.

29. The improvement of Claim 23, wherein the cavity of said fixture contains an analyte responsive element selected from the group consisting essentially of a solid, liquid or a gas.

30. The improvement of Claim 29, wherein the analyte responsive element includes a liquid absorbent medium and at least one reagent that is interactive with a constituent of the sample, an immunocomplex of an additional material and a constituent of the sample or a reaction product of the sample and an additional material.

31. In a test kit for constituent analysis of a fluid sample, said kit comprising a sample collection device, a chemistry reagent system specific for interaction with a constituent suspected of being present in the fluid sample and written instructions for performance of an analysis of said fluid sample,

the improvement comprising

(a) a kit package in the form of a hinged, transparent box, which includes the sample collection device and all of the reagents specific for performance of constituent analysis of a fluid obtained with said device, and

(b) instructions for arrangement of said kit components relative to indicia in said package, so as to incorporate said written instructions for performance of said assay into a work station array of said kit components relative to indicia

in said kit package.

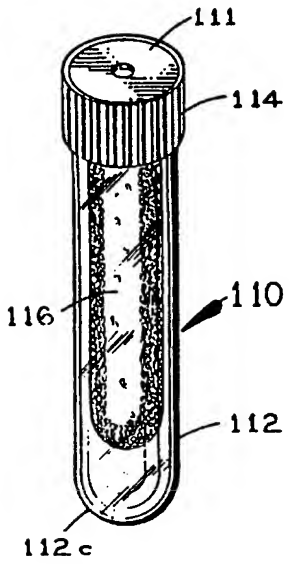


FIG. 1

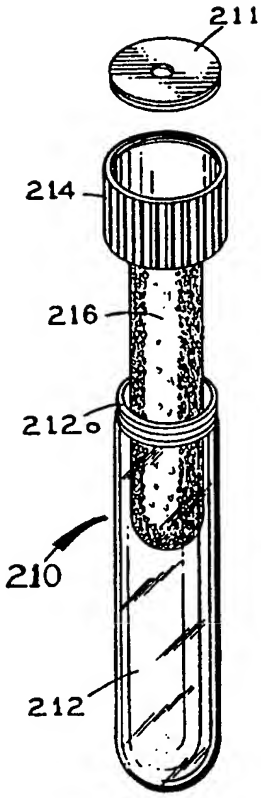


FIG. 2

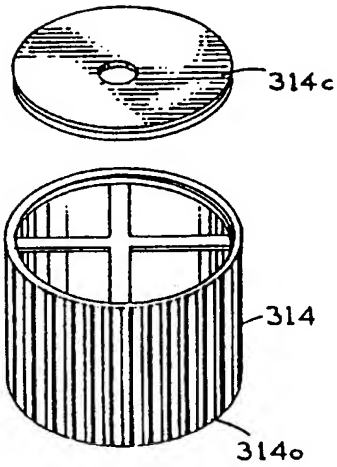


FIG. 3A

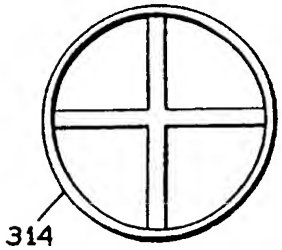


FIG. 3B

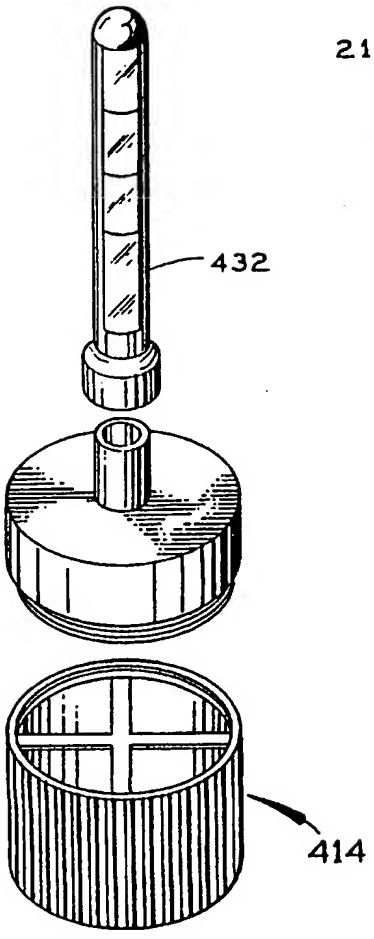


FIG. 4B

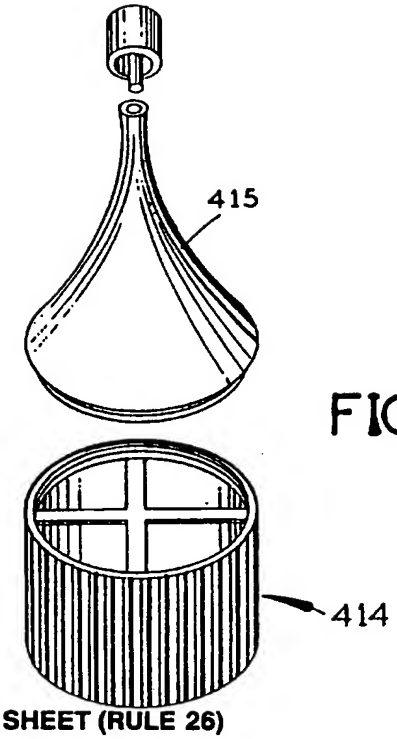


FIG. 4A

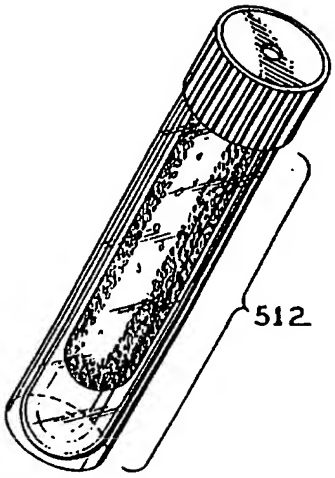


FIG. 5

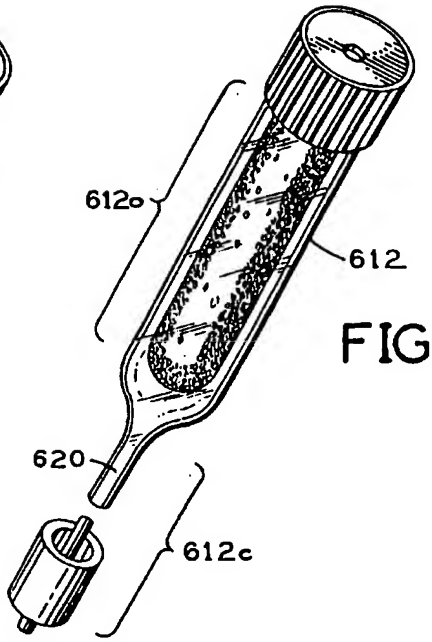


FIG. 6A

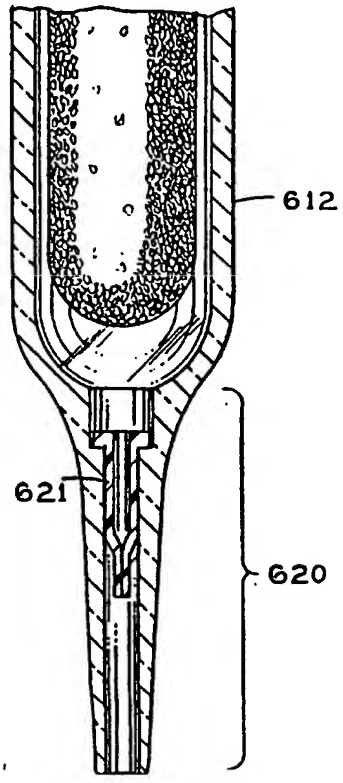


FIG. 6B

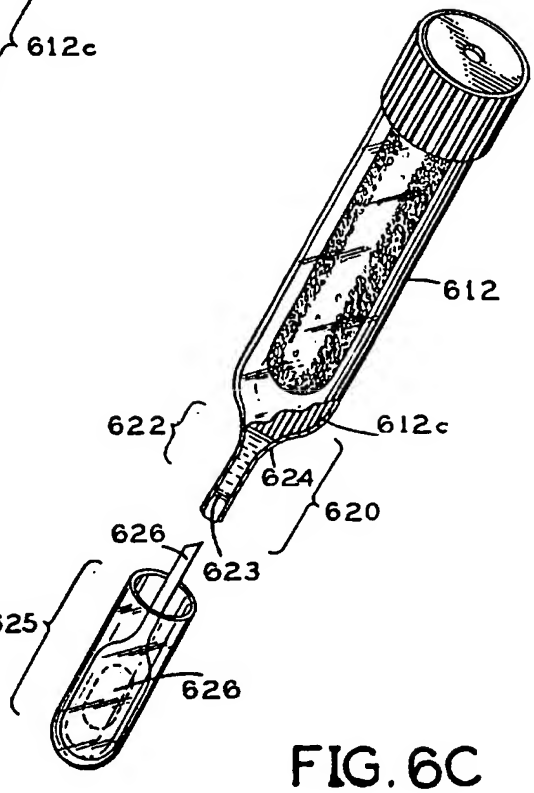


FIG. 6C

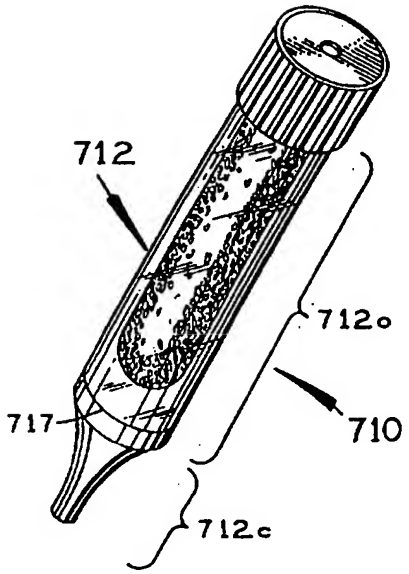


FIG. 7A

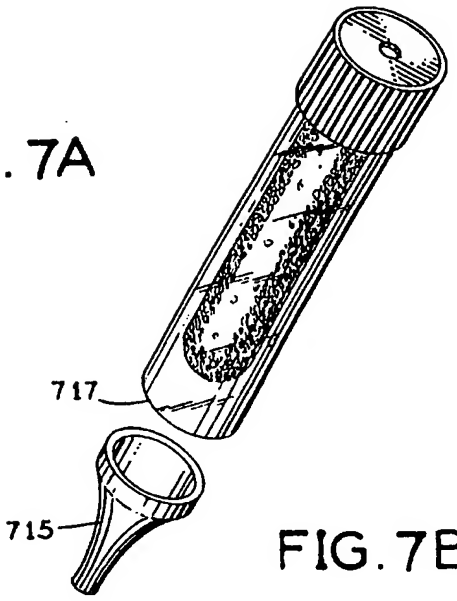


FIG. 7B

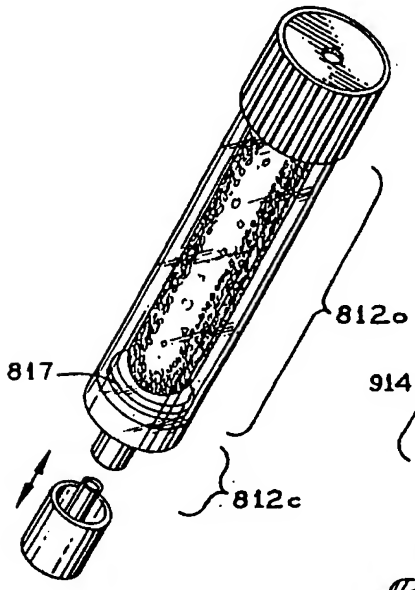
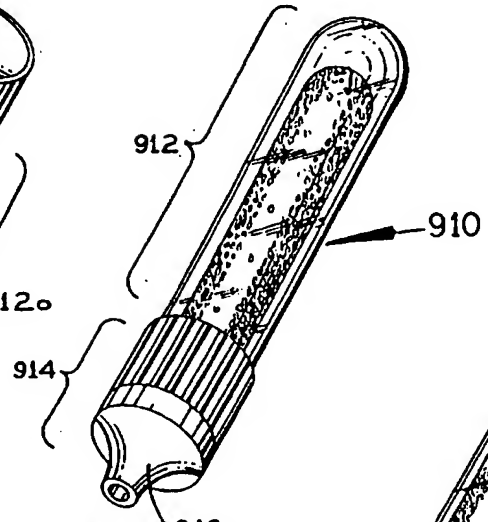


FIG. 8A



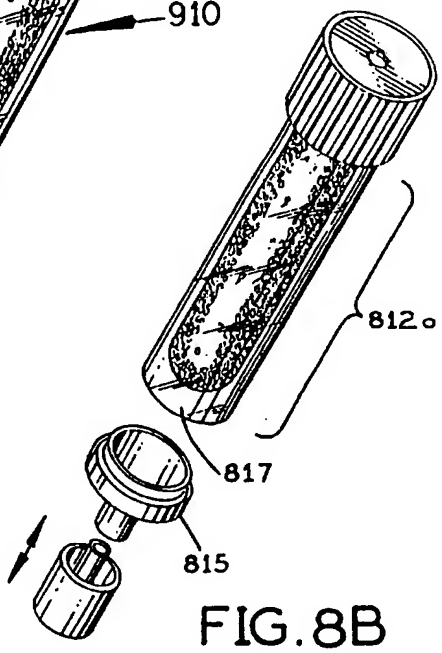


FIG. 8B

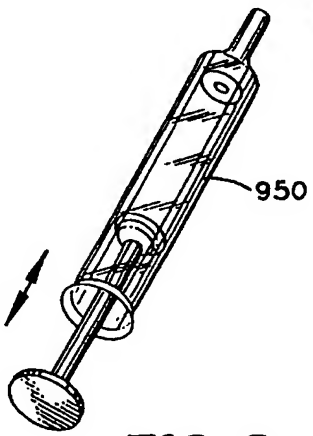


FIG. 9

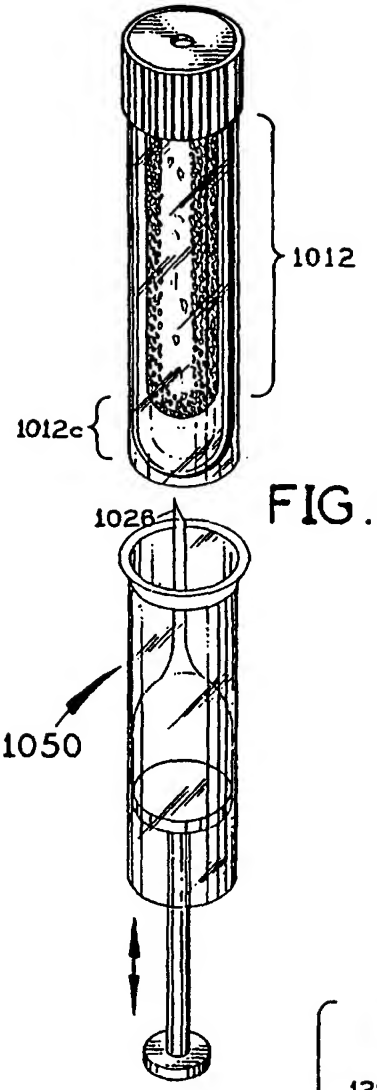


FIG.10

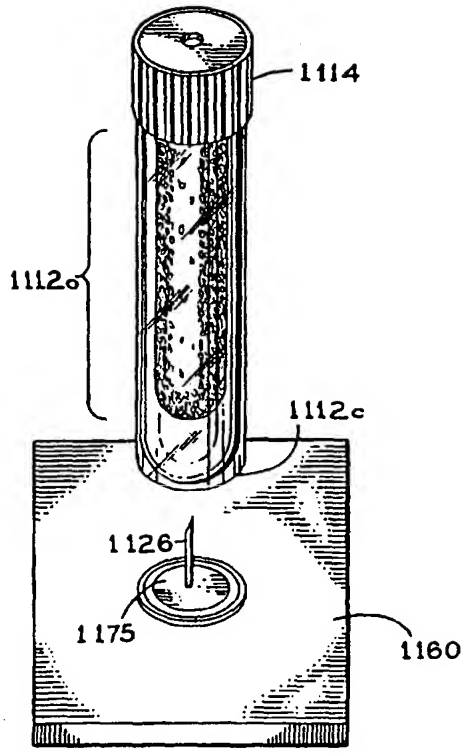


FIG.11

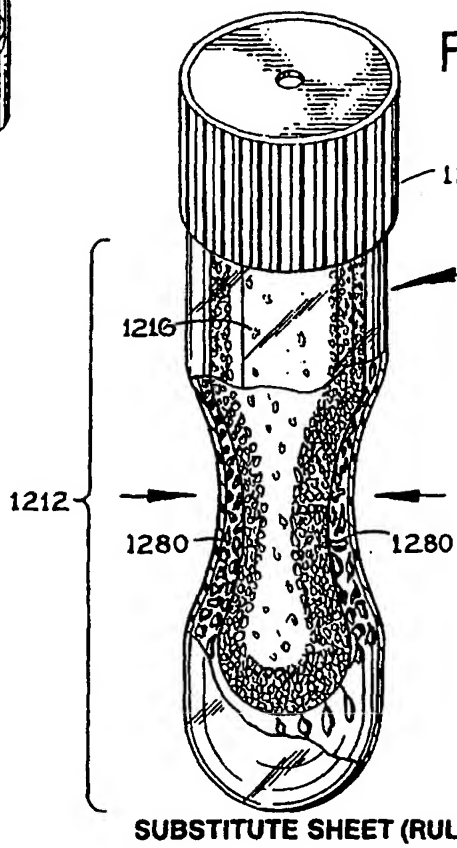


FIG.12

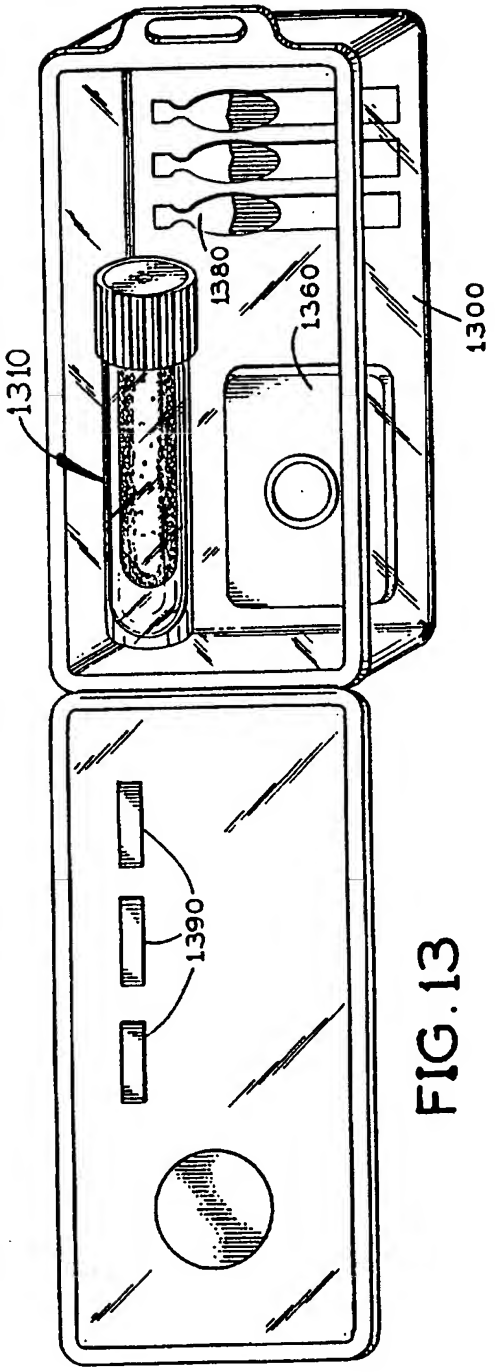


FIG. 13

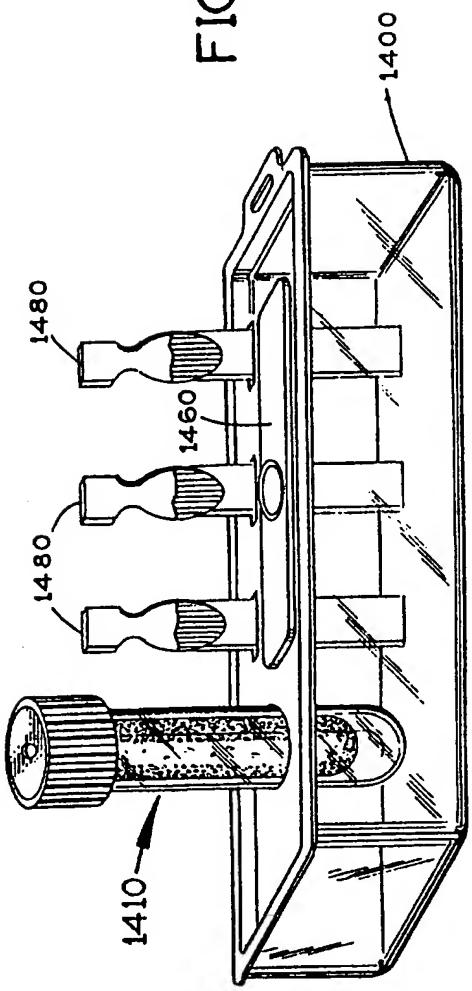


FIG. 14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/16075

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :B01L 3/14
US CL :422/102
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/68.1, 84, 85, 86, 88, 101, 102, 104

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EPA 0,383,262 A2 (YAMAZAKI et al) 13 February 1990, see entire document.	1-3, 7-8, 10-13, 17, 19-23, 27, 29-30
Y	US 5,103,836 A (GOLDSTEIN et al) 14 April 1992, see entire document.	4-6, 9, 14-16, 18, 24-26, 28, 31
Y	US 4,873,193 A (JENSEN et al) 10 October 1989, see entire document.	4-6, 9, 14-16, 18, 24-26, 28, 31
A,P	US 5,543,115 A (KARAKAWA et al) 06 August 1996, see entire document.	1-31
A	US 5,334,502 A (SANGHA) 02 August 1994, see entire document.	1-31

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
15 JANUARY 1997

Date of mailing of the international search report
21 FEB 1997

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/16075

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,211,182 A (DEUTSCH et al) 18 May 1993, see entire document.	1-31
A	US 4,956,298 A (DIEKMANN) 11 September 1990, see entire document.	1-31
A	US 4,600,507 A (SHIMIZU et al) 15 July 1986, see entire document.	1-31
A	US 4,418,702 A (BROWN et al) 06 December 1983, see entire document.	1-31
A	EPA 0,539,141 A1 (HAMAGUCHI) 28 April 1993, see entire document.	1-31